Signaling by FGFR2b controls the regenerative capacity of adult mouse incisors.

Journal: Development

Publication Year: 2010

Authors: Sara Parsa, Koh-Ichi Kuremoto, Kerstin Seidel, Reza Tabatabai, Breanne Mackenzie, Takayoshi Yamaza, Kentaro Akiyama, Jonathan Branch, Chester J Koh, Denise Al Alam, Ophir D Klein, Saverio Bellusci

PubMed link: 20978072

Funding Grants: Laying the groundwork for building a tooth: analysis of dental epithelial stem cells

Public Summary:
Rodent incisors regenerate throughout the lifetime of the animal owing to the presence of epithelial and mesenchymal stem cells in the proximal region of the tooth. Enamel, the hardest component of the tooth, is continuously deposited by stem cell-derived ameloblasts exclusively on the labial, or outer, surface of the tooth. The epithelial stem cells that are the ameloblast progenitors reside in structures called cervical loops at the base of the incisors. Previous studies have suggested that FGF10, acting mainly through fibroblast growth factor receptor 2b (FGFR2b), is crucial for development of the epithelial stem cell population in mouse incisors. Our results demonstrate that FGFR2b signaling regulates both the establishment of the incisor stem cell niches in the embryo and the regenerative capacity of incisors in the adult. We intend to use the insights provided by our experiments in mice to guide us in the use of stem cells in regenerating dental tissues.

Scientific Abstract:
Rodent incisors regenerate throughout the lifetime of the animal owing to the presence of epithelial and mesenchymal stem cells in the proximal region of the tooth. Enamel, the hardest component of the tooth, is continuously deposited by stem cell-derived ameloblasts exclusively on the labial, or outer, surface of the tooth. The epithelial stem cells that are the ameloblast progenitors reside in structures called cervical loops at the base of the incisors. Previous studies have suggested that FGF10, acting mainly through fibroblast growth factor receptor 2b (FGFR2b), is crucial for development of the epithelial stem cell population in mouse incisors. To explore the role of FGFR2b signaling during development and adult life, we used an rtTA transactivator/tetracycline promoter approach that allows inducible and reversible attenuation of FGFR2b signaling. Downregulation of FGFR2b signaling during embryonic stages led to abnormal development of the labial cervical loop and of the inner enamel epithelial layer. In addition, postnatal attenuation of signaling resulted in impaired incisor growth, characterized by failure of enamel formation and degradation of the incisors. At a cellular level, these changes were accompanied by decreased proliferation of the transit-amplifying cells that are progenitors of the ameloblasts. Upon release of the signaling blockade, the incisors resumed growth and reformed an enamel layer, demonstrating that survival of the stem cells was not compromised by transient postnatal attenuation of FGFR2b signaling. Taken together, our results demonstrate that FGFR2b signaling regulates both the establishment of the incisor stem cell niches in the embryo and the regenerative capacity of incisors in the adult.